REMARKS

Claims 1, 3-10, 13, 14, 17, 18, 24, 28, 30, 34, 36, 40, 42, 48, 52, 56, 60 and 66-69 are pending in the application. Claims 3-10, 64 and 65 have been withdrawn from consideration. Applicants wish to point out that claims 3-10 were incorrectly listed in the prior paper submitted October 27, 2005. Claims 3-10 are now properly shown in the above claim listing.

Claims 1, 13, 14, 17, 18 and 66-69 have been allowed. Claims 24, 28, 30, 34, 36, 40, 42, 48, 52, 58 and 60 are rejected. Claims 24, 28, 30, 34, 36, 40, 42, 48, 52, 56 and 60 have been newly canceled without prejudice or disclaimer. Applicants reserve the right to file one or more continuation, divisional and/or continuation-in-part applications directed to the canceled subject matter and/or any other subject matter disclosed in the instant specification.

Claims 70-120 have been newly added to more particularly define the subject matter of the application and to correct minor grammatical errors. Support for newly added claims is as follows:

Support for claim 70 may be found in the specification Examples 31-37, pages 76-83, paragraphs 000369-000396 and Example 45, pages 92-92, paragraphs 000425-000431.

Support for claims 71, 75, 79, 83 and 87 may be found in original claim 13.

Support for claims 72, 76, 80, 84 and 88 may be found in original claim 15.

Support for claims 73, 77, 81, 85 and 89 may be found in original claim 17.

Support for claims 74, 78, 82, 86 and 90 may be found in original claim 19.

Support for claim 91 may be found in original claim 24.

Support for claims 92-96 may be found in original claim 25.

Support for claims 97-98 may be found in original claims 26-27.

Support for claims 99, 101, 103, 105, and 107 may be found in original claim 28.

Support for claims 100, 102, 104, 106, and 108 may be found in original claim 29.

Support for claim 109 may be found in original claim 48.

Support for claims 110-114 may be found in original claim 49.

Support for claims 115 may be found in original claim 50.

Support for claims 116-120 may be found in original claim 51.

No new matter has been introduced by these amendments. Reconsideration and allowance of the remaining claims in view of the amendments above and remarks below are respectfully requested.

Claim Rejections – 35 U.S.C. § 112

Claims 24, 28 and 48 are newly rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite. The Examiner contends that the specification does not set forth any steps for determining how to identify "diseases in which insulin resistance is the underlying pathophysiological mechanism." Applicants have canceled claims 24, 28 and 48, thereby rendering the rejection with respect to these claims moot, Newly added claims do not contain the language which the Examiner found objectionable. Thus, reconsideration of this basis for rejection is respectfully requested.

Claims 24, 28, 30, 34, 36, 40, 42, 48, 52, 56 and 60 remain rejected under 35 U.S.C. § 112, second paragraph as allegedly not enabled. Claims 30, 34, 36, 40, 42, 52, 56 and 60 have been canceled, thereby rendering the rejection with respect to these claims moot. With respect to claims 24, 28, and 48, the Examiner contends that the specification, while enabling treatment of type II diabetes, insulin resistance, psoriasis and hypercholesterolemia, does not reasonably provide enablement for the treatment of other conditions recited in the claims. Applicants respectfully traverse this basis for rejection.

Applicants have canceled claims 24, 28 and 48, thereby rendering the rejection with respect to these claims moot. Newly added limit the recited diseases to hyperlipidemia, hypercholesteremia, hyperglycemia, insulin resistance, psoriasis, obesity, leptin resistance and type II diabetes. With respect to type II diabetes, insulin resistance, psoriasis and hypercholesterolemia, the Examiner has already

indicated that the specification enables the treatment of these diseases. With respect to hyperlipidemia and hyperglycemia, Applicants submit that the specification also enables the treatment of these diseases. The specification clearly describes the reduction of blood glucose and triglyceride levels following *in vivo* administration of the claimed compounds. (*See* p. 100, ¶ 453 to p.105, ¶ 471.) The specification therefore enables one skilled in the art to treat these conditions. Thus, reconsideration of this basis for rejection is respectfully requested. With respect to obesity and leptin resistance, applicants assert that the paragraphs [0006] to [0013] of the specification provide materials and data that impart enabling support for the treatment of obesity and leptin resistance. Applicants would further wish to draw the Examiner's attention to applicant's arguments and the references submitted with the previous response and amendment filed on March 1, 2004. Based on the specification and the information in the references it is clear that one skilled in the art knows of the relationship between the effects of PPAR alpha and/or PPAR gamma on obesity, and leptin resistance Attached is a copy of Applicants arguments and remarks filed on March 1, 2004.

It is believed that claims 1, 13, 14, 17, 18 and 66-120 are now in condition for allowance, early notice of which would be appreciated. No fee is believed due at this time. If, however, any additional fees are due, the Commissioner is authorized to charge any such fee to our Deposit Account No. 50-3221.

Respectfully submitted,

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REMARKS

Claims 1-65 are pending in this application. Claims 1 and 3 have been amended to delete the phrase "its derivatives, its analogs, its tautomeric forms." Therefore, it is respectfully requested that the rejection of claims 1, 2 and 12-63 under 35 USC 112, second paragraph and claims 1, 2, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60 and 62 under 35 USC 112, first paragraph be withdrawn.

Paragraph [00451] has been amended to exchange the headings of PPAR gamma with concentration in the 4th and 5th columns.

The Examiner has rejected claims 20-23, 30-41, and 52-59 under 35 USC 112, first paragraph, as not being enabled. Applicants respectfully traverse this rejection.

Applicants submit that the claims are enabled. The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation. United States v. Telectronics, Inc. 8 USPQ2d 1217, 1223 (Fed. Cir. 1988). A patent need not teach, and preferably omits, what is well known in the art. In re Buchner, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991). As explained below, one skilled in the art knows of the relationship between impaired glucose tolerance, insulin resistance and/or the effect of PPAR alpha and/or PPAR gamma on obesity, renal diseases, psoriasis, polycystic ovarian syndrome, leptin resistance and cancer. Based on this information and the disclosure in the specification it is clear that the claims are enabled.

Renal Diseases

Page 866 of the Chapter Endocrinology and Reproduction, Textbook of Medical Physiology, Eighth Edition, Arthur C. Guyton (W.B. Saunders Company).

In column 1 of this page it is stated "Because complications of diabetes-such as atherosclerosis, greatly increased susceptibility to infection, diabetic retinopathy, cataracts, hypertension, and chronic renal disease-are more closely associated with the level of the blood lipids than with the level of blood glucose, it is the object of some clinics to administer sufficient glucose and insulin so that the quantity of blood lipids becomes normal." This reference teaches the relationship between blood lipids and renal diseases. Therefore, since the compounds of this invention reduce blood lipids, the treatment of renal diseases is enabled.

Ma, L.J. et al. Kidney Int. 2001 May; 59(5):1899-910 teaches that PPAR gamma beneficial effects are independent of insulin/glucose effects and are associated with regulation of glomerular cell proliferation... Therefore, since the compounds of this invention are ligands of PPAR gamma, the treatment of glomerular cell proliferation which is a renal disease is enabled.

Cancer

Pershadsingh, H. 131:317180, Expert. Opin. Invest. Drugs, 8(11), 1859-1872, 1999 describes that PPAR gamma agonists can promote apoptosis, block angiogenesis and inhibit pathol. remodelling in a variety of malignant and non-malignant pathol. states." This reference suggests that PPAR gamma agonists can be used for the treatment of cancer.

Kopelovich, L. Mol. Cancer. Ther. 2002 Mar; 1(5):357-63 discloses that activation of PPAR gamma and inhibition of PPAR delta may prevent cancer. "PPAR gamma agonists induce differentiation, inhibit the growth of established tumor cells in vitro and in vivo and have chemopreventive effects modies. PPARalpha has anti-inflammatory and differentiating activity and protects against the oxidative damage associated with aging. ...This review presents a rationale for using PPAR modulators as cancer chemopreventive drugs." Since the compounds of this invention are ligands of PPAR alpha and PPAR gamma, the treatment of cancer is enabled.

Dementia

Watson, G.S. et al. CNS Drugs 2003: 17(1):27-45 describes evidence that "suggests that an increased prevalence of insulin abnormalties and insulin resistance in Alzheimer's disease may contribute to the disease pathophysiology and clinical symptoms." The abstract also discloses that the insulin plays a role in memory functions. It is stated in the abstract that "The increased occurrence of insulin resistance in Alzheimer's disease and the numerous mechanisms through which insulin may affect clinical and pathological aspects of the disease suggest that improving insulin effectiveness may have therapeutic benefit for patients with Alzheimer's disease."

Claude Messier, et al. Behavioural Brain Research 75(1996):1-11. This paper discusses the relationship between Alzheimer's disease and glucose and concludes in the second column on page 7 "There are indications that treatment of altered glucoregulation in AD patients with anti-diabetic drugs could lead to small but significant improvements in cognitive function."

Therefore, since it has been shown that the compounds of this invention can be used to treat insulin resistance, the treatment of dementia is enabled.

Obesity

Michaela Modan, J. Clin. Invest. Vol. 75, March 1985, 809-817 discusses the relationship between impaired glucose tolerance and obesity.

Koutnikova H., Ann. N.Y. Acad. Sci. 2002 Jun.: 967:28-33 describes the relationship between PPAR gamma and obesity.

Therefore, since the compounds of this invention are ligands of PPARgamma, the treatment of obesity is enabled.

PCOS

Nestler, John E. 131:128241 Contemp. Endocrinol. 12:347-365, 1999 is the abstract of a review that reviewed 95 refs. and concluded that the evidence supports the pathogenic role of hyperinsulinemia in polycycstic ovary syndrome (PCOS). This abstract describes the correlation of hyperinsulinemia and PCOS.

Wyne, Kathleen, et al. 130:204564, Curr. Opin. Endocrinol. Diabetes, 5(4), 321-329, 1998 Lippincott Williams & Wilkins is the abstract of a review of 40 references. "This article reviews new developments in the field of polycystic ovarian syndrome and insulin resistance and focusing on the inter-relationship of the two syndromes.

Legro, R.S. 129:342122, Rev. Argent. Endocrinol. Metab. 35(1), 22-41, 1998 discloses that PCOS is associated with significant insulin resistance as well as with defects in insulin secretion. "The initial investigational use of insulin-sensitizing agents in these [PCOS] women has shown favorable response. Therefore, since it has been shown that the compounds of this invention, can be used to treat insulin resistance and impaired glucose tolerance, the treatment of PCOS is enabled.

Psoriasis

Ellis, C.N. et al. Arch. Dermatol. 2000 May; 136(5):609-16 teaches that ligands for PPAR gamma inhibited the proliferation of normal and psoriatic human keratinocytes in culture. Since the compounds of this invention are ligands of PPAR, the treatment of psoriasis is enabled.

Leptin Resistance

Andrea Dunaif, Chapter 9, Insulin Resistance and Ovarian Dysfunction, pages 301-Insulin In regard to leptin resistance, the examiner's attention is drawn to paragraph [00013] of this application.

Jens C. Bruning, et al. Science 2000;289:2122-2125.

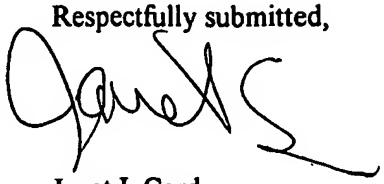
According to page 2124 of this article, there is an interesting link between insulin and leptin action in the regulation of body weight.

Given this information and the information in the specification, the claims are in compliance with the enablement requirement and it is respectfully requested that the rejection be withdrawn.

The Examiner has rejected claims 1, 2 and 11-63 under the judicially created doctrine of obviousness type double patenting. This rejection will be addressed when the Examiner indicates that claims of this application are allowable.

Accordingly applicants submit that the present application is in condition for allowance and favorable consideration is respectfully requested.

Respectfully submitted,



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